



**UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office**

Address: COMMISSIONER OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

10

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
-----------------	-------------	----------------------	---------------------

08/486,070      06/07/95      STAVRIANOPOULOS      J      ENZ-7(P)(C3)

HM12/0907

RONALD C FEDUS  
ENZO DIAGNOSTICS, INC  
C/O ENZO BIOCHEM, INC.  
527 MADISON AVENUE, 9TH FLOOR  
NEW YORK NY 10022

EXAMINER

MARSCHER, A

ART UNIT	PAPER NUMBER
----------	--------------

1631

29

DATE MAILED:

09/07/00

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

Application No.  
08/486,070

Applicant(s)

Stavrianopoulos et al.

Examiner

Ardin Marschel

Group Art Unit

1631



☒ Responsive to communication(s) filed on several dates

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1035 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claim

☒ Claim(s) 183-318 and 325-717 is/are pending in the applicat

~~Of the above, Claim(s) 1-182 and 319-324 have been canceled. ~~are withdrawn from consideration~~~~

☐ Claim(s) \_\_\_\_\_ is/are allowed.

☒ Claim(s) 183-318 and 325-717 is/are rejected.

☐ Claim(s) \_\_\_\_\_ is/are objected to.

☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.

## Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some\* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_

☒ Interview Summary, PTO-413 (7 copies)

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

The amendment, filed 11/23/98, crossed in processing at the PTO with the mailing of the final action, mailed 12/8/98. To add to the confusion the final action, mailed 12/8/98, was returned by the Post Office to the PTO as undeliverable due to addressing error. Due to this amendment crossing in processing, the Post Office return of the final action, and due to the newly added rejections hereinbelow summarized; the finality of the office action, mailed 12/8/98, is hereby withdrawn and the response time is restarted as of the mailing of this office action.

The art unit designated for this application has changed. Applicant(s) are hereby informed that future correspondence should be directed to Art Unit 1631.

In order to expedite prosecution; the Applicants' arguments and amendments, filed 11/23/98, 5/19/99, 7/30/99, 8/20/99, 11/1/99, and 12/10/99; have been entered and have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

If applicant desires priority under 35 U.S.C. § 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. It is noted that this appears as the first sentence

of the specification following the title. The status of non-provisional application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. \_\_\_\_\_" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application. It is noted that the relationship between 06/732,374 and 06/461,469 in said paragraph at the beginning of the instant specification is as a continuation. Reviewing the relationship as printed on U.S. Patent 4,994,373 has revealed that the Patent gives this relationship as continuation-in-part. Applicants are requested to review the parentage history for the instant application and reconcile or correct any discrepancies.

Claims 189-192, 196, 205-207, 233-236, 245-247, 275, 277-280, 293-295, 325-376, 379, 381, 382, 387, 389, 390, 395, 397, 398, 405, 407-410, 414, 423-425, 451-454, 463- 465, 493, 495-498, 502, 511-513, 539, 541, 542, 547, 549, 550, 555, 557, 558, 565, 567-570, 574, 582-584, 610-613, 621-623, 651, 653-656, 660, 668-670, 696, 698, 699, 704, 706, 707, 712, 714, and 715 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had

possession of the claimed invention.

A thorough review of the instant application has revealed that several of the claims now contain NEW MATTER which was not disclosed as filed. The following NEW MATTER limitations are listed with the respective claims in which they are contained directly or due to dependence from a claim which contains the NEW MATTER. It is noted that basis was pointed to for many of these limitations in the amendment, filed 5/19/99. These are commented on below as appropriate. It is additionally noted that this 5/19/99 amendment cited previous claims as support for several presently pending claims, but that none of these previous claims were original claims but rather claims which were filed after the originally filed disclosure. It is regretted that the NEW MATTER was not pointed out earlier in these claims.

In claims 325-376 arrays are claimed. These claimed arrays start with the broadest versions in claim 325 as only requiring a substrate surface with double-stranded nucleic acid fixed or immobilized thereto with at least one strand labeled as described in said claim. The closest array description, as filed, is given in the specification on page 16, lines 9-27. In this description the array also is limited to glass plates having depressions or wells with denatured analytes deposited therein, wherein single stranded analytes are fixed to the surfaces of the wells. Chemically labeled probes may then be hybridized to these

analytes and subjected to detection of any probe-analyte hybrid. It is noted that the analytes are characterized as being "various" which supports the presence of "different" analytes deposited in each well or depression. It is additionally noted that plastic wells are a disclosed option as given in the bridging sentence between pages 20 and 21 of the instant specification. Polystyrene microfilter wells are described on page 22, lines 10-12, as a solid support. The practice of fixing polynucleotide analytes to conventional microtiter plates is described on page 23 at the start of Example 7. In summary, the array embodiments, as filed, are all at least directed to solid supports with wells or depressions therein. It is lastly noted that instant claim 325 does not require either wells or depressions as being the form of the array of analyte fixation sites nor its being either glass or plastic, wherein microtiter arrays are deemed to be made of plastic. It is additionally noted that arrays of tubes or cuvettes as given in claim 340 has not been found as filed. Thus, the broader arrays as included in claim 325 contains NEW MATTER. Such broader array embodiments which are NEW MATTER, for example, include flat surface arrays or non-glass or non-plastic arrays. This NEW MATTER is contained in instant claims 325-376.

The solid support given as "nitrocellulose" is cited in the instant specification on page 10, line 23, but the broader term

"cellulose" has not been found as filed. This broader limitation which contains NEW MATTER in the additional breadth over the more limited "nitrocellulose" is present in instant claims 275, 336, 375, 376, 405, 414, 493, 502, 565, 574, 651, and 660.

Several of the instant claims contain the limitation given as "glass-coated". This limitation is NEW MATTER in that glass-coated indicates a solid support which has a coating of glass over it. This coating type has not been found as filed. It is noted that coatings of various types are instantly disclosed such as coating of a solid support with a material which permits linkage, fixation, or immobilization of analytes, for example. Thus, the coating is not glass per se but rather optionally a linker coating on a glass solid support. The phrase "glass-coated" is indicative of a solid support having a glass coating thereon which is NEW MATTER in instant claims 189, 190, 196, 233, 234, 277, 278, 338-341, 375, 376, 407, 408, 414, 451, 452, 495, 496, 502, 567, 568, 574, 610, 611, 653, 654, and 660.

Several of the instant claims contain the limitation given as "plastic-coated". This limitation is NEW MATTER in that plastic-coated indicates a solid support which has a coating of plastic over it. This coating type has not been found as filed. Thus, similar to the above glass-coated NEW MATTER, the plastic-coated NEW MATTER is present in instant claims 191, 192, 196, 235, 236, 279, 280, 409, 410, 414, 453, 454, 497, 498, 502, 569,

570, 574, 612, 613, 655, 656, and 660.

Several of the instant claims contain the limitation given as "oncogene" or combination thereof containing an oncogene. This limitation is NEW MATTER in that the limitation, oncogene, has not been found as filed. The amendment, filed 5/19/99, referred to the reference EP 63879 for support for these limitations. The next paragraph, below, explains why this is improper incorporation by reference and supports this rejection. The following claims contain this NEW MATTER: 205, 206, 245, 246, 293, 294, 348, 349, 375, 376, 423, 424, 463, 464, 511, 512, 582, 583, 621, 622, 668, and 669.

Several of the instant claims contain limitation directed to specific types of mutations given as deletion, insertion, inversion, point mutation, and a combination thereof. These limitations are NEW MATTER in that the limitations have not been found as filed. It is noted that the amendment, filed 5/19/99, indicated that these mutation types could be found in the publication EP 63879, cited on pages 7-8 of the instant specification. Consideration of this page 7-8 citation reveals that it was cited as a reference which reviewed non-radioactive signalling and bridging/signalling systems. It was not cited for any other disclosure. This is an incorporation by reference of pointed to subject matter but not other subject matter. Such incorporations by reference must be directed to particular



disclosures for them to be usable for giving written basis for claim limitations. A specific claim limitation is clearly essential subject matter. It is improper to incorporation by reference essential subject matter cited in a foreign patent application. It is improper to generically cite such a reference and then utilize it for anything therein without defining in the citation what it is cited for. In this case the publication was cited for non-radioactive signalling etc. review and not for mutation types. Thus, it does not serve as a proper basis for incorporating mutation types into the instant claims. For further discussion, see the M.P.E.P. at section 608.01(p), part I, subsection A. The following claims contain this NEW MATTER: 206, 246, 294, 349, 375, 376, 424, 464, 512, 583, 622, and 669.

Several of the instant claims contain the limitation given as "partially double-stranded". This limitation is NEW MATTER in that the limitation has not been found as filed. In the amendment, filed 5/19/99, Examples 1-7 were cited for support. Consideration of said Examples 1-7 has failed to reveal written basis for this limitation. The following claims contain this NEW MATTER: 207, 247, 295, 345, 375, 376, 425, 465, 513, 584, 623, and 670.

Several of the instant claims contain the limitation given as "aminopropyltriethoxysilane". This limitation is NEW MATTER in that the closest limitation as filed is given as the more

limited material: gamma-aminopropyltriethoxysilane. This material is cited in the instant specification on page 15, lines 26-27. The added breadth of this material without also being of the "gamma" type is NEW MATTER. The following claims contain this NEW MATTER: 328, 375, 376, 379, 387, 395, 539, 547, 555, 696, 704, and 712.

Several of the instant claims contain the limitation given as "a dispersive compound". This limitation is NEW MATTER because this broad concept of a dispersive compound has not been found as filed. The following claims contain this NEW MATTER: 330, 331, 375, 376, 381, 382, 389, 390, 397, 398, 541, 542, 549, 550, 557, 558, 698, 699, 706, 707, 714, and 715.

Claims 183-318 and 377-717 are rejected, as discussed below, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Comparison of instant claims 183 and 185 causes both claims to be vague and indefinite as to what is meant for the claimed subject matter. In claim 183, line 2, the system is described as being non-porous but confusingly the claim lacks any actual items in the system which are then pointed to as being non-porous. Also, there is no indication whether the non-porous limitations in claim 183 are meant for all system items or only a portion of the system. Claims 185-187 then further confuse the system

characterization in that the solid support has therein a porous option. In reviewing the instant specification, the solid support in claim 183 seems to be the only overtly cited item in the claimed system that would be reasonably described as corresponding to the non-porous item in line 2 of claim 183, but, in conflict, it limited as an option to being porous in claim 185. Clarification as to what metes and bounds such as actual system items are non-porous in claim 183 is requested via clearer claim wording, including clarifying what is non-porous in the practice of the system of claims 185-187 when the solid support is porous. This same concern exists for claims 231, 271, 401, 449, 489, 561, 608, 647, and those dependent therefrom as confusingly mixing porous and non-porous limitations.

Claim 184 is vague and indefinite as to what is meant by the solid support both being within the system as well as being a part of the system due to its dependence from claim 183. Other similar dependent claims are rejected hereinunder due to this issue, such as claim 272 etc. Clarification via clearer claim wording is requested.

Claim 188 is vague and indefinite in defining a selection of options but does not clarify whether the solid support is therein limited to being the non-porous option from claim 185.

Claims 204 and 205 cite the phrase "to be identified" which lacks antecedent basis in claim 183 from which they depend

because only quantitation is cited in said claim 183. Claims dependent from claim 204 also contain this antecedent basis issue. Claims 244, 245, 292, 293, 422, 423, 462, 463, 510, 511, 581, 582, 620, 621, 667, 668, etc. also contain this issue. Similarly, claims 229, 269, 317, 447, 487, 535, 606, 645, 692, and claims dependent therefrom cite "detectable" which lacks antecedent basis due to only quantitation being cited in claims from which they depend.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 561-563, 571, 574, 575, 577, 578, 580-582, 585-609, 612-614, 617, 619-621, 624-649, 652, 655-657, 660, 661, 663, 664, 666-668, and 671-693 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Kourilsky et al. (UK 2,019,408).

As previously described of record Kourilsky et al. discloses the centrifugal fixation of a target/probe hybrid with a chemical

label thereon on page 3, lines 18-54, with evaluation of bound probe via a  $\beta$ -galactosidase in solution of the resuspended hybrids. Instant claim 561 requires at least three items: a solid support, fixed double-stranded oligonucleotide or polynucleotide, and a chemical label which may be quantified in solution via dye, chromogen, enzyme, etc. given the complex character of the label of Kourilsky et al. These items are cited above as being disclosed by Kourilsky et al. The quantitation limitations in instant claim 561, for example, is a capability which clearly is present considering the solution enzyme determination of Kourilsky et al. and thus is anticipated by the reference, even though Kourilsky et al. does not perform the quantitation while the hybrids are still fixed on the support. Also, centrifuge tubes for such a centrifugal procedure are well known to be made of translucent, non-porous, plastic. Several added instant limitations directed to various bridging moieties and immobilization via hybridization of the probe are deemed anticipated by the the somewhat complex assemblage of the probe/target hybrid and label moieties in that portions are direct, portions are indirect, etc. The probe is clearly immobilized via hybridization. Otherwise the assay would be non-functional if non-hybridized probe also was fixed by the centrifugation step.

Claims 183-185, 188, 189, 197-201, 203-205, 208-223, 225-227, 229-233, 240, 241, 243-245, 248-263, 265-267, 269-273, 276, 277, 285-289, 291-293, 296-311, 313-315, 317, 318, 377, 385, 393, 401-403, 406, 407, 415-419, 421-423, 426-441, 443-445, 447-451, 458, 459, 461-463, 466-481, 483-485, 487-491, 494, 495, 503-507, 509-511, 514-529, 531-533, 535-537, 545, 553, 561-563, 566, 567, 575-578, 580-582, 585-600, 602-604, 606-610, 617, 619-621, 624-639, 641-643, 645-649, 652, 653, 661-664, 666-668, 671-686, 688-690, 692-694, 702, and 710 are rejected under 35 U.S.C. § 102(e) as being clearly anticipated by Stuart et al. (P/N 4,732,847) or Ward et al. (P/N 4,711,955).

Stuart et al. discloses the practice of in-situ hybridization on a coverslip with fluorescent antibody detection of probe/target hybrids in column 6, lines 17-57, which anticipates the above instant claims. The target samples were prepared on acid washed microscope slides as indicated in column 4, lines 61-67. The slides and coverslips at the time were well known to be transparent glass and non-porous and form a system. The acid washing is deemed a surface treatment as required in instant claim 377, for example. The fluorescent labeling is deemed a type of chemical label because instant dependent claims such as claim 221 includes fluorescent labeling in the signalling limitations. It is noted that Stuart et al. does not disclose quantitation of signal but it is also noted that the instant

claims are directed to a capability for quantitation of label and are not method claims. A fluorescent label as utilized in Stuart et al. emits light which is well known to be quantifiable and thus anticipates the instant claims listed above. See the below paragraph which cites legal decisions as to shifting the burden to applicants to distinguish the reference disclosure over the invention when the claimed subject matter is expected to anticipate the claimed invention by having properties cited in the instant claims but not measured in a cited prior art reference. Ward et al. also cites in-situ hybridization with detection with avidin-peroxidase in columns 19-20 therein which reads on the above claims also due to the eminent quantifiability of such signals.

It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

No claim is allowed.

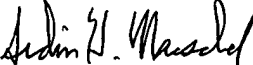
Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703) 308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to the Technical Center receptionist whose telephone number is (703) 308-0196.

August 22, 2000

  
ARDIN H. MARSCHEL  
PRIMARY EXAMINER



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Jannis G. Stavrianopoulos, et al.	)	Group Art Unit: 1807
Serial No.	08/486,070	)	Examiner: Ardin H. Marschel, Ph.D.
Filed:	June 7, 1995	)	
Title:	COMPOSITION EMPLOYING CHEMICALLY LABELLED OLIGONUCLEOTIDE OR POLYNUCLEOTIDE, AND KIT AND APPARATUS CONTAINING SAME	)	

527 Madison, 9th Floor  
New York, New York 10022  
September 5, 2000

Honorable Commissioner  
of Patents and Trademarks  
Washington, D.C. 20231

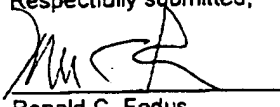
**POWER TO INSPECT AND MAKE COPIES**

Dear Sirs or Mesdames:

The undersigned is an attorney of record for Applicants in the above-identified application.

It is hereby authorized that Patsy M. Paxton and/or Brian Willingham, 2001 Jefferson Davis Highway (Suite 1003), Arlington, VA 22202, be permitted to inspect and make copies of U.S. Serial No. 08/486,070 filed June 7, 1995, and to make formal inquiry as to the status of this application.

Respectfully submitted,



Ronald C. Fedus  
Registration No. 32,567  
Attorney for Applicants

ENZO DIAGNOSTICS, INC.  
c/o ENZO BIOCHEM, INC.  
527 MADISON AVENUE, 9TH FLOOR  
NEW YORK, NY 10022  
TEL. (212) 583-0100

Enz-7(P)(C3)

lic/power to inspect Enz 7(P)(C3)

RECEIVED  
SEP 13 1600/2900  
00 SEP 13 PM 1:42